REMARKS

Claims 1, 2, 40, and 66-68 are pending in the application. Claim 40 has been cancelled. Claims 1, 2 and 66 have been amended. Support for the amendments to claims 1, 2 and 66 can be found in the specification at page 123, lines 10-25 and page 114 lines 1-10, and in Figure 4A. New claims 69-71 have been added. New claims 69 and 70 recite the peptide dimers of this invention and support for these claims can be found in the specification at page 123, lines 10-25 and page 114 lines 1-10, and in Figure 4A. New claim 71 has been added to recite the addition of affinity tags (V5, His 6 or both) as described in the examples, *e.g.*, Example 2, p. 113 ln 27 - p. 114 ln 16. No new matter has been added.

Claim Rejections Under 35 U.S.C. §102(e)

Claims 1, 2, 40, and 66-68 have been rejected as being anticipated by Gilbert *et al.*, US 6,495,668 B1 ("Gilbert"). Applicants traverse. Applicants have submitted herewith the Declaration of Dr. Catherine Burgess (Burgess Decl. ¶ __) in support of the arguments made herein.

Claim 40 has been cancelled, and the rejection is moot as it applies to that claim.

Claims 1, 2 and 66, as amended, (and new claims 69 and 70) recite a composition of polypeptide dimers of associated peptide fragments consisting of C-terminal fragments of SEQ ID NO:2, specifically amino acid residues 247-370, 249-370, 247-338 and 339-370, where the composition appears as a protein of about 35 kDa under non-reducing conditions and appears as bands I, II, and III under reducing conditions, wherein bands II and III are cleavage fragments of band I and where the composition induces proliferation of fibroblasts. In Example 12, applicants show purification of intact and cleaved products of the 30664188.m99 protein. Under reducing conditions SDS-PAGE shows three bands of molecular weight 22-25kDa (band I), about 16kDa (band II) and about 5-6kDa (band III). Further, as Example 12 shows, N-terminal amino acid analysis of these fragments determines that band I and II begin with cleavage at residue 247 and band III begins at residue 339.

Gilbert describes many peptide fragments of varying lengths and spanning various portions of the PGDF-D full length molecule. See col. 12, lines 22-34. The Examiner has noted that Gilbert points out the general boundaries of the CUB domain, the interdomain region and the

growth factor domain. The Examiner focuses on disclosure in Gilbert that refers to the beginning of the growth factor domain at amino acid residues 258-370 and argues that "this domain may include residues 250 to 370 or 246 to 370." See Gilbert, col. 9, lines 39-44. The Examiner also notes that Gilbert goes on to state that the domain boundaries can be expected to vary by up to plus or minus 5 residues from these positions. Burgess Decl. ¶ 9.

However, of the many peptides specifically recited in Gilbert, Gilbert simply does not teach the specifically recited peptide compositions claimed here. Burgess Decl. ¶ 6, 8.

First, Gilbert does not disclose the amino acid sequence of peptide fragments 247-338 and 339-370 at all. These are required elements of the claims here. Burgess Decl. ¶ 11. For this reason alone, the claims cannot be anticipated by Gilbert.

Nor does Gilbert disclose a peptide dimer of the associated fragments consisting of amino acids 247-370, 249-370, 247-338 and 339-370. Burgess Decl. ¶ 12. For this reason alone, the claims cannot be anticipated by Gilbert.

As Dr. Burgess states, there are multiple factors that are involved in generating a bioactive PGDF-D peptide dimer composition as claimed here – specifically, the peptides have to be expressed, secreted, and assembled to form an active dimer. Specifically, based on her experience with PGDF-D peptides, she concludes that the ordinarily skilled artisan would have no reasonable expectation of success in predicting whether any particular PGDF-D peptide dimer would be bioactive based solely on its amino acid sequence. Burgess Decl. ¶ 14. Dr. Burgess goes on to note that based on her experience in working with various peptide fragments of PGDF-D, even minor changes (e.g., addition of one or more amino acids or addition of a affinity tag) at the N-terminus or C-terminus may have very significant effects on dimerization, aggregation and bioactivity. Because of this, it is not possible to predict from Gilbert which of the many fragments recited in Gilbert are bioactive and which are not, including which peptides within Gilbert's 246-370 fragment plus or minus 5 residues are bioactive. Burgess Decl. ¶ 14.

As the foregoing makes clear, minor changes in PGDF-D dimers have significant consequences on the operability of PGDF-D peptide dimers. Gilbert provides no basis for selecting between the operable (bioactive) and non-operable embodiments of the many theoretical PGDF-D peptides listed. And Gilbert provides no basis for selecting the particular PGDF-D peptide dimer compositions claimed here. The claims cannot be anticipated by Gilbert.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for a three month extension of time and associated fee under 37 C.F.R. §1.17(a)(3) accompanies this response. The Commissioner is authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 15966-577 (CURA-77).

Respectfully submitted,

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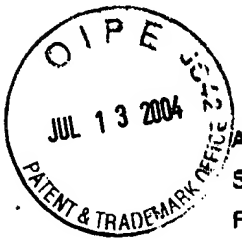

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Shimkets *et al.*		
SERIAL NUMBER:	09/662,783	EXAMINER:	Dong Jiang
FILING DATE:	September 12, 2000	ART UNIT:	1646
FOR:	GROWTH FACTOR POLYPEPTIDES AND NUCLEIC ACIDS ENCODING SAME		

DECLARATION OF CATHERINE E. BURGESS UNDER 37 C.F.R. § 1.132

I, CATHERINE E. BURGESS, declare and state that:

1. I received a Bachelor of Science degree in biology from Old Dominion University in Norfolk, Virginia in 1987, and a Ph. D. degree in Biomedical Sciences from Eastern Virginia Medical School, Department of Biochemistry in 1994;

2. I am currently employed at CuraGen Corporation in New Haven, Connecticut, as a Senior Project Manager, Exploratory Development, the assignee of this patent application;

3. I am the holder of one (1) United States Letters Patent, and a named co-inventor on more than fifty (50) pending United States patent applications; and an author of thirteen (13) scientific papers which appear in Journals such as the *BMC Neurology, Cytogenet. Genome Res., Nat. Cell Biol., Cancer Res., Int. J. Mol. Med., Am. J. Hum. Genet; and Biochim. Biophys. Acta;* and four (4) book chapters in, for example, Methods in Molecular Genetics (CRC Press), and Laboratory Protocols for Mutation Detection (Oxford Press);

4. I have read and am familiar with the specification and claims of United States Patent Application USSN. 09/662,783 entitled "Growth Factor Polypeptides and Nucleic Acids Encoding Same", including the January 13th 2004 Office Action in which pending Claims 1, 2, 40 and 66-68 were deemed to be unpatentable under 35 U.S.C. § 102(e) as being anticipated by United States Patent No. 6,495,668 issued to Gilbert et al. ("Gilbert");

5. I have been asked by Patent Counsel to review the specification and claims in USSN 09/662,783, the January 13th 2004 Office Action, and the Gilbert reference, and have done so;

6. I have concluded after my review that there are a number of distinctions that can be made between the teaching of the Gilbert citation and the claimed subject matter of USSN 09/662,783 which, in my opinion and belief, do not render the claimed subject matter of USSN 09/662,783 anticipated by the Gilbert teaching;

7. I have noted that the pending claims in USSN 09/662,783 are drawn to compositions of polypeptide dimers of associated peptide fragments consisting of C-terminal fragments of the SEQ ID NO:2 peptide which, when analyzed by SDS-PAGE under non-reducing conditions yielded a band of an apparent molecular weight of 35 kDa, and under reducing conditions three bands were detected: band I at 22 to 25 kDa, band II at 16 kDa, and band III at 5 to 6 kDa which subsequent N-terminal analysis showed that bands I and II began at amino acid residue No. 247 and band III began at amino acid residue No. 339 of SEQ ID NO:2, and that the polypeptides corresponding to bands II and III are cleavage fragments of the polypeptides corresponding to band I, where the composition induces proliferation of fibroblasts;

8. I have been unable to locate any teaching or suggestions in Gilbert that specifically recites the polypeptides fragments claimed in USSN 09/662,783 and that are listed in paragraph 7, above.

9. I have also noted that the January 13th 2004 Office Action indicates that Gilbert points out the general boundaries of the CUB domain, the interdomain region, and the growth factor domain, and focuses on disclosure in Gilbert that refers to the beginning of the active growth factor domain being the result of cleavage of the full-length gene product containing the amino acid residues 258 to 370, and states that "this domain may include residues 250 to 370 or 246 to 370." (see Gilbert at column 9, lines 39 – 44) and the domain boundaries can be expected to vary by up to plus or minus 5 residues from these positions (see, Gilbert at column 4, lines 15 - 16);

10. It is my opinion and belief that it is not possible to predict, with the reference before me, which of the many peptides encompassed by the teaching of Gilbert (i.e., amino acid residue 246 to 370 plus or minus 5 amino acid residues) would have the bioactivity of the specific molecules being claimed in USSN 09/662,783;

11. I note that Gilbert does not disclose the specific amino acid sequence of the peptides (amino acid sequences corresponding to positions 247 to 338, and 339 to 370) encompassed by the claims in claims of USSN 09/662,783;

12. I note that Gilbert does not disclose a peptide dimer of the associated fragments consisting of amino acid sequences taken from positions 247 to 370, 249 to 370, 247 to 338, and 339 to 370, which are encompassed by the claims in claims of USSN 09/662,783;

13. It is my opinion and belief that Gilbert does not recognize the claimed peptide dimer compositions of the invention described and claimed in USSN 09/662,783;

14. Based upon my experience with PGDF-D peptides: (1) I am aware that there are multiple factors involved in generating a bioactive PGDF-D peptide dimer composition as claimed in USSN 09/662,783, specifically, the peptide needs to be expressed, secreted, and assemble to form an active dimer, (2) I am of the view that the ordinarily skilled artisan would not have a reasonable expectation of success in predicting whether any particular PGDF-D peptide dimer would be bioactive based solely on its amino acid sequence, (3) I am of the opinion that even minor changes (e.g., addition of one or more amino acids or addition of a affinity tag) at the N-terminus or C-terminus may have significant effects on dimerization, aggregation, expression, and bioactivity, and because of these beliefs I am of the belief and opinion that it is not possible to predict from the disclosure contained in Gilbert which of the many fragments recited therein would have or not have bioactivity, including those peptides which would fall within Gilbert's 246 to 370 amino acid fragment plus or minus 5 residues disclosure;

15. For each of the reasons stated herein, it is my belief and opinion that the peptides being claimed in USSN 09/662,783 are not encompassed by the Gilbert reference, and that there is nothing stated in Gilbert that would lead one of ordinary skill in the art to make those specific peptides encompassed in the claims of USSN 09/662,783 and expect them to have the bioactivities reported in the application.

16. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Catherine E. Burgess

Catherine E. Burgess

Signed this day 13 of July, 2004